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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	6

DATE MAILED: 11/01/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/927,395	LIVSHITS ET AL.	
	Examin r	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/396,357* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-5 are presently pending in this application.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/396,357, filed on 9-15-99.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Claim Objections

Claim 2 is objected to because of the following informalities: Claim 2 recites the phrase "of 557 to 1171 of" in line 4. Examiner notes that the recitation of the first word "of" is grammatically improper and suggests deletion of the said word. Appropriate correction is required.

Claim 3 is objected to because of the following informalities: Claim 3 recites the phrase "in a cell of said bacterium" in lines 3 and 4. Examiner notes that the said phrase is redundant and suggests deletion of the above phrase. Appropriate correction is required.

Claim 4 is objected to because of the following informalities: Claim 4 recites the phrase "in the cell of said bacterium" in line 3. Examiner notes that the said phrase is redundant and suggests deletion of the above phrase. Appropriate correction is required.

Claim 5 is objected to because of the following informalities: Claim 5 recites the phrase "in the cell of said bacterium" in line 3. Examiner notes that the said phrase is redundant and suggests deletion of the above phrase. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 1 and claim 2 dependent on claim 1 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 1 is drawn to "A DNA coding for..." which reads on a product of nature. Amending the claim to recite "An isolated polynucleotide...." to show the hand of man would overcome this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the

invention. Claim 2 recites the phrase "under stringent conditions". A perusal of the specification provides a definition which is very vague or incomplete. Stringent conditions are clearly defined in the art in terms of salt concentrations required in the hybridization and wash buffers and the temperature at which hybridization and wash is performed (see Maniatis et al.). Therefore the use of the above phrase renders the claim indefinite. Based on the exemplary reference provided as a part of the definition of the "stringent conditions", Examiner has examined the above claims as those claiming polynucleotides which are 70% homologous to nucleotides 557-1171 of SEQ ID NO:1.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for DNA with SEQ ID NO:1 or nucleotides 557 to 1171 encoding a polypeptide which renders the cells in which the DNA is expressed, homoserine resistant, does not reasonably provide enablement for any DNA which encodes a polypeptide comprising an amino acid sequence including deletion, substitution, insertion or addition of one or several amino acids (variants, mutants and recombinants) in SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1)

the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-5 are so broad as to encompass any DNA which is a variant, mutant or a recombinant of SEQ ID NO:1 from any or all sources and vectors and host cells (*E.coli*) comprising such DNAs. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of DNA sequences that are broadly encompassed by the claims.

Applicants propose to use the above polynucleotides for a variety of processes such as recombinant cells for production of amino acids. Since the nucleotide sequence determines the type of protein and the ultimate function of the encoded protein and since only nucleic acids with very high percent homology can be used for the above purpose, changing the nucleotide sequences as proposed by the applicants and/or addition of substantial amount of additional nucleotide sequence unrelated to the nucleic acid sequence of SEQ ID NO:1 may not lead to desired function of the polynucleotides. This is because the changes suggested by the applicants will result in an enormous number of nucleotide sequences that may or may not encode the polypeptide which renders the cells resistant to homoserine. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of a polypeptide with the above property.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or modifications of nucleotides, as encompassed by the instant

claims, and the base changes within a nucleic acid's sequence can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given DNA to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any DNA encoding a protein which imparts homoserine resistance because the specification does not establish: (A) regions of the DNA sequence which may be modified without effecting the above mentioned activity/utility; (B) the general tolerance of homoserine resistance imparting DNA sequence to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleotide sequence with an expectation of obtaining the desired biological function and utility; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any or all DNA which are variants, mutants or recombinants of SEQ ID NO:1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of DNAs having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-5 are directed to polynucleotides encoding polypeptides corresponding to the sequence of SEQ ID NO:2 in which one or several amino acids are deleted, substituted or inserted and host cells with such polynucleotides. Claims 1-5 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polynucleotides encoding polypeptides derived from SEQ ID NO:2 including modified polypeptide sequences, modified by one or several deletions, additions, insertions and substitutions of an amino acid residue in SEQ ID NO:2 that have not been disclosed in the specification. No description has been provided of the modified polynucleotides encoding the polypeptide sequences encompassed by the claim in terms of its structure. No information, beyond the characterization of SEQ ID NO:1 encoding SEQ ID NO:2 has been provided by applicants which would indicate that they had possession of the claimed genus of polynucleotides encoding modified polypeptides. The specification does not contain any disclosure of the structure of all the polynucleotides encoding polypeptide sequences derived from SEQ ID NO:2, including fragments and variants within the scope of the claimed genus. The genus of polynucleotides claimed is a large variable genus including polynucleotides which can have a wide variety of structure and function. Therefore many structurally and functionally unrelated polynucleotides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species

within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-5 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-5 of copending Application No. 09/847,392. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Conclusion

None of the claims are allowable.

Examiner has found nucleotide sequences and polypeptide sequences in the prior art (GenBank Database Accession No. M87049 and P27847 for DNA and polypeptide respectively) matches for SEQ ID NO:1 (99.5% match) and SEQ ID NO:2 (66.1% match). However,

Examiner has not used these reference to reject claims 1-5 as being anticipated or obvious since both the reference do not identify the function of the DNA and polypeptide sequence and simply list them as either "function unknown" or as "hypothetical 15.4 K.D. protein in RecQ-PldB intergenic region (f138) in *E.coli*". These references are however considered as references of interest to the above application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.

MANJUNATH RAO
PATENT EXAMINER

Manjunath N. Rao
October 30, 2002